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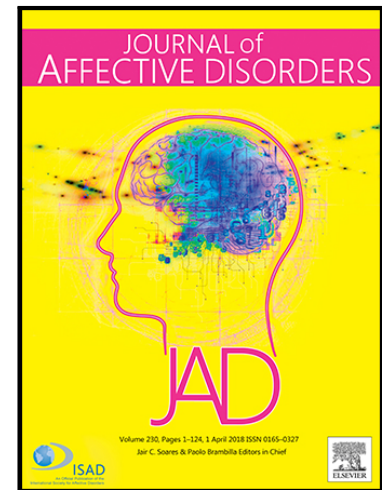
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## Accepted Manuscript

OpenSIMPLE: A real-world implementation feasibility study of a smartphone-based psychoeducation programme for bipolar disorder

Diego Hidalgo-Mazzei , María Reinares , Ainoa Mateu ,  
Viktoriya L Nikolova , Caterina del Mar Bonnín , Ludovic Samalin ,  
Aitana García-Estela , Víctor Pérez-Solá , Allan H. Young ,  
Sergio Strejilevich , Eduard Vieta , Francesc Colom

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## Highlights

- So far, many mental health internet-based platforms (IBP) were developed and tested.
- Few of these IBPs were made widely available for mental health patients.
- OpenSIMPLe evaluated the large-scale implementation of an IBP for bipolar disorder.
- Positive outcomes regarding satisfaction, usability and helpfulness were found.
- Attrition rates were high, requiring further research about retention factors.

# OpenSIMPLe: A real-world implementation feasibility study of a smartphone-based psychoeducation programme for bipolar disorder

Diego Hidalgo-Mazzei, MD, PhD<sup>1,2</sup>; María Reinares, PsyD, PhD<sup>2</sup>; Ainoa Mateu, PsyD<sup>3</sup>; Viktoriya L Nikolova, PsyD, MRes<sup>1</sup>; Caterina del Mar Bonnín, PsyD, PhD<sup>2</sup>; Ludovic Samalin, MD, PhD<sup>4</sup>; Aitana García-Estela, PsyD, MSc<sup>5</sup>; Víctor Pérez-Solá, MD, PhD<sup>5</sup>; Allan H. Young, MD, PhD<sup>1</sup>; Sergio Strejilevich, MD<sup>6</sup>; Eduard Vieta, MD, PhD<sup>2\*</sup>; Francesc Colom, PsyD, MSc, PhD<sup>5</sup>

<sup>1</sup> Centre for Affective Disorders, Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, United Kingdom.

<sup>2</sup> Bipolar Disorder Unit, Institute of Neuroscience, Hospital Clinic, University of Barcelona, IDIBAPS, CIBERSAM, Barcelona, Catalonia, Spain.

<sup>3</sup> Centre for Psychiatry, Division of Brain Sciences, Department of Medicine, Imperial College London, London, United Kingdom.

<sup>4</sup> Department of Psychiatry, CHU Clermont-Ferrand, University of Auvergne, EA 7280, Clermont-Ferrand, France.

<sup>5</sup> Mental Health Group, IMIM (Institut Hospital del Mar d'Investigacions Mèdiques)-Hospital del Mar, CIBERSAM, Barcelona, Catalonia, Spain.

<sup>6</sup> Bipolar Disorder Programme, Neurosciences Institute, Favaloro University, Buenos Aires, Argentina.

**Keywords:** Smartphone, bipolar disorder, psychoeducation, SIMPLe, intervention, upscale, implementation.

**Running title:** An implementation feasibility study of an e-mental health programme.

**\*Corresponding author:** Eduard Vieta, Bipolar Disorders Program, Neurosciences Institute, Hospital Clínic de Barcelona, IDIBAPS, CIBERSAM, Universitat de Barcelona, Villarroel 170, 08036. Barcelona, Catalonia, Spain. Tel. (34) 93 227 54 00. Fax. (34) 93 227 92 28. E-mail: [evieta@clinic.ub.es](mailto:evieta@clinic.ub.es).

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## Abstract

**Background:** Few evidence-based mental health apps are widely available to patients and, conversely, many of the available apps haven't been appropriately evaluated. Given that the ultimate goal is to scale-up and open Internet-based platforms (IBP), it is crucial to appropriately evaluate their real-world feasibility beforehand. We aimed to evaluate the implementation feasibility of a smartphone-based psychoeducational programme for bipolar disorder, exploring its long-term retention, usability, perceived helpfulness and satisfaction, alongside its impact on secondary health outcomes.

**Methods:** Participants were recruited via the project website after completing an online screening questionnaire. They were requested to complete web-based questionnaires before using the app and after 6 months of use which included sociodemographic, illness and treatment variables, the World Health Organisation-Five Well-Being Index (WHO-5) and the Short Form Health Survey (SF-36). The follow-up questionnaires also contained satisfaction and usefulness questions.

**Results:** 201 participants took part in the study. According to their retention, 66.2% of the participants were classified as non-completers and 33.8% as completers. The only predictor significantly associated with higher odds of retention was older age (OR=1.021,  $p < 0.001$ ). 62% of the users reported they were satisfied with the programme with a higher percentage among completers. WHO-5 baseline and follow-up scores showed a significant improvement as well as 6 out of 8 domains of the SF-36.

**Limitations:** Screening and outcome measures were administered using exclusively self-reported online methods.

**Conclusion:** The 6-month attrition rate of the programme was high. Positive outcomes regarding satisfaction were found predominantly among completers. The optimal dosage and retention of IBP mental health programmes remain challenging issues that need further research.

**Keywords:** Smartphones; bipolar disorder; psychoeducation; SIMPLE; mental health; implementation.

## Introduction

The high prevalence of mental health disorders in comparison to the limited availability of traditional healthcare resources has led to an increasing interest in new cost-effective methods which could meet this growing demand and burden (Kessler et al., 2007; Whiteford et al., 2013). Given their growing, ubiquitous and broad accessibility, Internet-based platforms (IBP) have frequently been proposed as a potential solution for reaching wider populations and increasing large-scale availability of health services, while simultaneously reducing costs. Thus, over the last twenty years, several projects have explored the possibility of providing adjunctive interventions through a wide array of e-mental health approaches for the most prevalent mental disorders (Lal and Adair, 2014).

Despite the initial optimism around IBPs in the mental health field and some positive findings regarding their efficacy, few projects have successfully implemented the platforms they evaluated (Buntrock et al., 2016; Firth et al., 2017; Wozney et al., 2017a). Most remained as research-only platforms never accomplishing their ultimate aim of becoming mental healthcare services in the real world (Meurk et al., 2016; Wozney et al., 2017a). Conversely, many platforms and smartphone applications (apps) which were not properly evaluated ended up being widely available mainly due to an increasing pressure of stakeholders (Ruwaard and Kok, 2015) and the lack of clear validation guidelines and policies to regulate these new technologies (Charani et al., 2014; Lewis and Wyatt, 2014; Torous et al., 2016). In fact, few of the currently available e-mental health apps provide contents in accordance with established self-management or practice guidelines standards (Bakker et al., 2016; Nicholas et al., 2015).

Among the most prevalent of mental health disorders, Bipolar disorder (BD) is a chronic, recurrent and disabling condition affecting more than 2% of the world population (Merikangas et al., 2011;

Whiteford et al., 2013). It consists of acute episodes of mood fluctuations and long-term sub-syndromal symptoms which have a significant negative impact on patients' quality of life, cognition, and life expectancy (Martínez-Arán et al., 2004; Michalak et al., 2005). In this context, SIMPLE (Self-monitoring and psychoeducation in patients with BD with a smartphone application) is a non-commercial academic project set out to develop and validate several IBPs and, amongst them, a self-management smartphone app for patients with BD. The app collects continuous information about symptomatology while offering personalized psychoeducation messages as an addition to treatment as usual in order to prevent relapses (Hidalgo-Mazzei et al., 2015). The psychoeducational contents are based on a face-to-face group psychological programme developed and extensively evaluated by our group (Colom et al., 2009; Colom and Vieta, 2006). It is worth mentioning that both efficacy and cost-effectiveness results were positive and the programme showed a significant reduction of the number of episodes to a half in the 5 years follow-up as well as improving other relevant clinical outcomes in BD (Colom et al., 2009). Unfortunately, despite being recommended as a first-line psychological treatment for maintenance in most international guidelines, the program did not make it in terms of implementation and dissemination. Hence, the ultimate goal of the SIMPLE project is to extend, personalize and facilitate the wide access to the psychoeducational contents of the programme around the world to everyone who may need it.

The early feasibility, acceptability, safety and user satisfaction of the first version of the app (SIMPLE 1.0) was evaluated in a 3-month study involving more than 50 patients with BD and showed positive and encouraging results (Hidalgo-Mazzei et al., 2016). Moreover, post hoc analyses also suggested some potential improvements in terms of the biological rhythms of the patients and medication adherence (Hidalgo-Mazzei et al., 2017). An independent and parallel randomized clinical trial (RCT) evaluating the efficacy of the second version of the app (SIMPLE+) is currently ongoing.

However, as is the case with other e-mental health interventions, one of the main issues noted during the feasibility study was the retention of participants (Ben-Zeev et al., 2016; Hidalgo-Mazzei et al., 2016). Although an acceptable 74% retention rate was attained at 3 months, the contents of our programme are intended to be delivered across a 6 months period. Therefore, the final implementation of a potentially widely available intervention could have been compromised if retention continued to drop. Moreover, upscaling of an open platform could potentially be affected by socio-demographic, cultural and technical factors (Aranda-Jan et al., 2014; Wozney et al., 2017b).

Considering the results of our initial feasibility study, the educational nature of the platform and requests from patients' associations and other Institutions to use an improved, modified and open version of the SIMPLE original app (i.e. SIMPLE 1.5) we decided to open the app to a wider population whilst remaining within an independent and parallel research protocol until conclusive results regarding its efficacy are available.

OpenSIMPLE is thus an implementation feasibility study using SIMPLE 1.5 aimed at evaluating the long-term retention, usability, perceived helpfulness and satisfaction among the first 201 users of the programme: a wider and more diverse population of patients with BD. Simultaneously, we set out to explore sociodemographic, self-reported clinical factors and technical factors influencing retention, while testing the system's capability in handling a larger number of users. Moreover, we explored secondary clinical outcomes related to general health and well-being among the app users.

## Methods



## The intervention: SIMPLe 1.5

The application offered to the participants in this study was an improved version of SIMPLe 1.0 (Hidalgo-Mazzei et al., 2016). Following the user-centred design approach adopted by the project (Hidalgo-Mazzei et al., 2015; McCurdie et al., 2012; Roth et al., 2014), in SIMPLe 1.5 we incorporated suggestions based on feedback received by patients during the feasibility study as well as modifications to adapt the platform for an open study. Additionally, we developed an iOS version with the same characteristics, which was not previously available.

In brief, the basic functionality of the app was similar to the first version. It consisted of a daily short graphic 5-item (mood, energy, sleep time, medication adherence and irritability) screening test and a weekly, more comprehensive YES or NO test, considering all DSM-5 criteria for manic and depressive episodes, including suicidal thoughts. Based on the information collected, a daily pop-up notification prompted the user to read a short psychoeducational message providing brief information or advice about how to deal with specific situations in order to avoid relapses. Each message was originally extracted from a library of more than 500 messages categorized according to different clinical situations based on published psychoeducational manuals for BD (Colom and Vieta, 2006). The educational messages were short and used plain language in order to ensure readability. A detailed description of the SIMPLe 1.0 app has previously been provided elsewhere (Hidalgo-Mazzei et al., 2016).

In addition to these functions, new features and characteristics were incorporated in SIMPLe 1.5 while at the same time it was stripped down from the main interventional components as follows:

- Medication reminders: The users could activate this module and choose from a list the medications they were taking and the time schedule. A pop-up notification prompted them

at the specified time to indicate whether they had taken their medication or not. Based on their answers a medication adherence score was calculated and, thus, the adherence question was omitted from the daily test. If the module was not activated, the medication adherence question remained in the daily test.

- Personalized prodromal symptoms: If this module was activated, after a brief tutorial to identify previous prodromal symptoms, the users could register their own past prodromal symptoms for each kind of episode. These were then added as an additional question in the weekly test.
- Gamification module: A basic virtual reward gamification module was implemented to encourage the engagement with the app. Depending on the number of tests completed and psychoeducational messages read each week, the users were awarded different medals (e.g. gold, silver, bronze, etc) and motivational messages. They could view the accumulated medals in a trophy gallery.
- Mood-chart sharing: Users could share their mood-chart graphic (not containing identifiable information) through e-mail.
- Psychoeducational messages community: The users could create and share anonymously their own advice and psychoeducational messages with the rest of the community. The messages were reviewed by mental health professionals (DH, FC), screened and cleaned from any potentially identifiable information, and added to the library in the correct category. The main aim of this feature was to replicate the sense of community and mutual collaboration of the face-to-face psychoeducational groups.

In order to comply with legal and ethical requirements as well as to moderate the interventional functions, the users were offered to configure their local emergency services telephone number and a reference e-mail of their preference. In the previous version these functions were not optional but instead linked to our clinic e-mail and local emergency services. Furthermore, although the initial versions of the app's mood scores showed acceptable correlations with the Young Mania Rating Scale (YMRS) and the 17-item Hamilton Depression Rating Scale (HDRS)(Hidalgo-Mazzei et al., 2016), minor improvements were made to the mood score calculation algorithm and redesigning the home-screen menu. Android and iOS versions were available only in Spanish.

## Procedure and participants

The option to participate in the study was available on the project website ([www.simplebipolarproject.org](http://www.simplebipolarproject.org)). No active online or direct advertisements were made by the researchers, except for leaflets explaining the study available at our bipolar disorders reference centre in Hospital Clinic and Hospital del Mar (Barcelona) and at Favaloro's Hospital Bipolar Disorder Programme clinic in Buenos Aires, Argentina. Patient associations' representatives who had contacted the team for the previous project were also notified of the availability of the study. The study included participants enrolled from May 2016 to August 2017.

The project's website contained information detailing the study purpose and eligibility criteria. Potential participants were requested to read and accept the conditions of participation in an informed consent (i.e. be  $\geq 18$  years, previously diagnosed with BD by a mental health professional, receiving direct and routine pharmacological treatment for their condition by a psychiatrist, currently owning and using daily an Android or iOS compatible smartphone, fully fluent in Spanish, with an active e-mail account and to complete a screening questionnaire). If they did not accept the conditions they were asked to state the main reason for declining participation. If they accepted,

potential participants were asked to complete a modified version of the Mood disorder questionnaire (MDQ)(Hirschfeld, 2002; Vieta et al., 2007). Based on their answers and using the same cut-off of the original MDQ, participants were informed whether they met the eligibility criteria for the study. We blocked the possibility to complete the questionnaire multiple times from the same IP address to prevent duplicate users and potential misuse.

## Assessments and measures

Following consent, participants were requested to fill out an online form containing: sociodemographic questions, illness and treatment history, the World Health Organisation-Five Well-Being Index (WHO-5) (Bonnín et al., 2018; World Health Organization, 2004) and the Short Form Health Survey (SF-36)(Turner-Bowker et al., 2012; Vilagut et al., 2005). After completing this information, participants were asked to provide a contact e-mail address. The responses were reviewed by a psychiatrist for consistency and within 72 hours an e-mail containing their personal six-digit alphanumerical access credentials was sent alongside instructions of how to download the app and log in. After 6 months of their inclusion in the programme, participants were prompted with an e-mail to complete a follow-up online questionnaire containing the WHO-5, SF-36, number of hospitalisations, suicide attempts and treatment history during the past 6 months. Episode density was calculated dividing the total number of previous episodes by the length of illness. The retention, use, engagement and subjective mood reported were collected from the data stored in the cloud server during the duration of the study. The engagement was calculated based on the weekly percentage of completed tasks (i.e. answering daily and weekly tests and reading the daily psychoeducational messages). Additionally, the follow-up questionnaire contained the system usability scale (SUS)(Brooke, 1996) as well as satisfaction and perceived helpfulness Likert scales. Technical support was provided to the users via e-mail throughout the duration of the study.

However, it was made clear that no advice regarding clinical status or treatment would be offered and this should be sought from their psychiatrist/psychologist.

The study was approved by the Ethical committees of the Hospital Clínic of Barcelona (HCB/2016/0403) and the Hospital del Mar - IMIM: Institut Hospital del Mar d'Investigacions Mèdiques (2016/6764/I).

## Data analyses

Descriptive analyses were conducted to characterize the sociodemographic and clinical characteristics of the initial sample as well as retention at the end of the programme, satisfaction and perceived helpfulness of each subcomponent of the app. Participants were further classified according to the total duration of app use as either non-completers ( $\leq 4.99$  months of use) and completers ( $\geq 5$  months of use). The lower-threshold for month usage was of at least 5 daily tests and 2 weekly tests completed within a month. This cut-off was set keeping in mind that, above 5 months, approximately 85% of the programme's essential contents would have been delivered which could be considered sufficient to enhance an initial therapeutic effect. Sociodemographic, clinical and treatment variables that could possibly affect retention were explored, performing Zero-Inflated Negative Binomial Regression analyses. An assessment of normality was performed to determine the distribution of the variables implicated in all analyses. Accordingly, non-parametric analyses were employed to compare the sample baseline and follow-up domains and total scores of the SF-36 and WHO-5, respectively, as well as suicide attempts and hospitalizations. Potential pre-post differences of these variables between completer and non-completers were also explored. Statistical significance was established at  $p = < .05$  level. All analyses were two-tailed and carried out using SPSS version 24.0 and zeroinfl R package.

## Results

Figure 1 detail the number of potential participants initially interested through to those included in and completing the project.

*[Figure 1 goes here]*

### Sociodemographic and clinical characteristics

After the screening process, two hundred and one subjects were included in the study. There was a preponderance of users from Spain (N=85), followed by Argentina (N=41), Chile (N=22) and Mexico (N=12). The mean age was 36.59 (SD=11) with a majority of female users (N=127, 63.2%) from a Latin-American origin (N=121, 60.5%) and with high education levels (N=126, 62.7%). A high percentage of the sample was actively employed at the time of the study entry (N=84, 41.8%) while only 20.9% were either in temporal (N=20) or permanent leave (N=22). Regarding housing conditions, more than half of the sample reported leaving independently, either owning (35.3%) or renting their current home (17.4%). Further sociodemographic variables of the sample are described in Table 1.

*[Table 1 goes here]*

Regarding the clinical characteristics, the sample reported a mean of 7.9 (SD=8.1) illness years, a significant number of previous manic/hypomanic (N=6.9, SD=3.3) and depressive episodes (N=6.2, SD=3.6), with a mean episode density of 0.8 (SD=1.9). Participants reported a high prevalence of both psychiatric and non-psychiatric comorbidities (N=123, 61.2%). Most of the subjects included were receiving treatment with at least one mood stabilizer (N=156, 77.6%) and at least one antipsychotic (N=129, 64.1%), while almost half of the sample was receiving at least one antidepressant (N=98, 48.7%). Further, 71% of the sample was receiving some kind of face-to-face

psychological treatment. More details about the clinical characteristics and treatments collected at baseline are described in Table 2.

*[Table 2 goes here]*

## Retention, use and engagement

The overall sample used the app for a median of 2 months (IQR 7). Thirty per cent (N=61) of the initial users remained interacting regularly with the app after 6 months. The attrition rate was 23.3 users per month. The highest number of drop-outs was observed during the first month when almost one-third (N=70, 34.8%) of users dropped out (Figure 2).

*[Figure 2 goes here]*

According to their retention, 133 (66.2%) patients were classified as non-completers and 68 (33.8%) as completers. A zero-inflated negative binomial logistic regression was performed to ascertain separately the effects of sociodemographic, clinical variables and treatment on participant retention. Among the sociodemographic variables, the only predictor significantly increasing the odds of retention was an increased age (OR=1.021, Coefficient=0.021, SE=0.00613,  $z=3.47$ ,  $p < 0.001$ , CI 95% = 0.0092-0.033). None of the clinical or treatment variables was found to have influenced long-term retention in the programme.

The overall average daily interaction of users while using the app was 1.8 times per day (SD=3.2). The average weekly engagement with the app of completers was as follows: 50 (25%) participants completed all tasks, 32 (16%) completed three-quarters, 30 (15%) completed half and 89 (44%) completed less than 25% of the tasks required. The average mood score reported by the participants during the study was -2.35 (SD=6.39), denoting based on our previous correlation with the HDRS and YMRS, a tendency to a slightly depressive mood. A detailed explanation of how these mood scores are calculated is provided in a previous study (Hidalgo-Mazzei et al., 2016). Only 72 (35.8%) of the

users activated the medication reminders module. 72 psychoeducational messages from the users were received, reviewed, adapted and added to the psychoeducational messages library.

### Usability, satisfaction and perceived helpfulness

One hundred and three participants (51.2%) responded to the follow-up questionnaire after 6 months of initiating the programme, of which fifty-six (54.4%) were non-completers. As per the usability, the mean SUS score of users who completed the follow-up questionnaire was of 77.23 (SD=16.7). An independent samples t-test showed that this score was significantly lower among non-completers ( $t(101) = -2.65, p = 0.09$ ).

Regarding the overall satisfaction of those who completed the follow-up questionnaire, 62% reported that they were either very satisfied or satisfied with the general experience of using the app with a significantly higher proportion among completers ( $\chi^2 = 5.58, p < 0.01$ ). Seventy percent strongly agreed or agreed that the app was easy to use. Likewise, almost the same percentage was reported regarding its daily use discretion and quickness, with 70% and 74%, respectively, strongly agreeing or agreeing about these aspects. No significant differences were found among the aforementioned variables between completers and non-completers.

In the follow-up questionnaire, we explored not only the general perceived helpfulness, but also which components of the app were considered by users to be most helpful in the self-management of their disorder. Users agreed that the most useful features were the mood chart, psychoeducational messages and daily tests, while the least useful were the gamification module, medication reminder, prodromal symptoms and mood chart sharing modules (Figure 3).

*[Figure 3 goes here]*



The most common reasons stated by participants for discontinuing app use were: repetitiveness and lack of time to complete tests (N=12), technical problems (N=9), lack of utility (N=7) and an undesired reminder of their condition (N=4).

Almost 85% of the participants responded they were willing to receive news about improved versions of the app in the future. The most frequently requested improvements were a personalized crisis plan in the case of relapse (N=71), the possibility to add personal stressful events in the mood chart (N=59), greater variety of psychoeducational messages (N=54), interactive mood-chart labels (N=38) and new methods to capture mood state without having to completed daily tests (N=33).

## Secondary clinical outcomes

Almost none of the baseline and follow-up measures showed a normal distribution, therefore we conducted non-parametric analyses to report and compare the pre-post results. The median WHO-5 baseline and follow-up scores were 40 (IQR 36) and 48 (IQR 32), respectively. A Wilcoxon Signed Ranks test ( $Z = -3.88$ ,  $p < 0.001$ ) was significant comparing both scores.

Similarly, the SF-36 showed significant differences between pre and post measures in 6 out of 8 domains: general health perceptions ( $Z = -2.92$ ,  $p < 0.01$ ), mental health ( $Z = -2.81$ ,  $p < 0.01$ ), physical role functioning ( $Z = -3.71$ ,  $p < 0.001$ ), emotional role functioning ( $Z = -5.12$ ,  $p < 0.001$ ), social functioning ( $Z = -3.37$ ,  $p < 0.001$ ), and bodily pain ( $Z = -2.92$ ,  $p < 0.05$ ).

No statistical significance was found regarding the number of hospitalisations, suicide attempts or other secondary clinical outcomes during the past 6 months between completers and non-completers.

## Discussion

The results of this study represent the first attempt to evaluate the feasibility of offering a large-scale wide-reaching smartphone-based IBP psychoeducation programme for BD. More than 30% of the participants continued to use the programme after 6 months. Positive outcomes regarding satisfaction and usability were mainly found among completers, whereas high percentages of perceived helpfulness, well-being and general health were found among all the participants. The data collected in this study provides significant insights into drop-out rate parameters, reasons and influencing factors of attrition which could help future platform design strategies and increase the chances of patient retention.

OpenSIMPLE is not the first study evaluating an IBP providing psychoeducational content to patients suffering from BD at a large scale. Barnes et al. (Barnes et al., 2007) previously developed a web-based relapse prevention programme ("Recovery Road") incorporating symptom monitoring and feedback, and psychoeducational elements. This consisted of symptom monitoring through questionnaires and mood charting with instant feedback on progress or recurrence risks alongside specific text-based psychoeducation and Cognitive Behavioural Therapy (CBT) contents. The programme was divided into 20 sequential sessions to be delivered in 12 months. An RCT compared the active programme with a control treatment containing only contents focused on general health. A case management system reminded the users in both groups to login into the sessions with three e-mails followed by a telephone call by a research assistant if necessary. No significant differences

were found between the intervention ( $n=113$ ) and the placebo ( $n=120$ ) groups regarding the main outcome, which was recurrences with or without hospitalization (Barnes et al., 2014). The retention rates reported were 75% for the active group and 69% for the control group at 12 months. In comparison to OpenSIMPLE which asked subjects to rate their mood and read brief psychoeducational messages daily, Recovery Road was less demanding in terms of the daily burden as sessions were delivered during specific weeks over a year. Additionally, the reminder e-mail system and telephone calls might explain the lower attrition rates in this study.

Using a slightly different approach, Lauder et al. conducted a 12-month randomized trial comparing head-to-head the clinical outcomes of two web-based programmes: "Moodswings", which contained psychoeducational material and discussion boards, and "Moodswings Plus" which also included elements of CBT (Lauder et al., 2014). The study recruited 156 participants, assigning 78 to each programme. They found significant reductions in mood symptoms and improvements in functionality, quality of life and medication adherence in both groups. However, the reported attrition rate at month 6 was 76% and 81% by month 12, which is greater although not dissimilar to the attrition rate observed in our study (66.2%). In a similar manner to our sample, most of the dropouts (65%) occurred during the first months of the programme, which suggests that the first months of any programme are the most critical in relation to long-term retention. It should also be noted that our programme was delivered through a smartphone-based platform, while the aforementioned interventions were web-based, which is also known to influence participants' engagement and expectations (Watts et al., 2013).

Smartphone app retention and engagement is not exclusively an e-mental health problem. It has been estimated that in general app retention rates are 36% after 1 month and just 20% after 3 months of use (Localitytics, 2018; Statista, 2016). Regarding health apps, the reported retention is

47% after 1 month and just 30% at 3 months (Farago, 2015). Studies specifically evaluating mental health apps for other chronic conditions have reported varied attrition rates ranging from 20% to as high as 75% (Arean et al., 2016; Donker et al., 2013; Firth and Torous, 2015; Grist et al., 2017).

One of the most likely factors affecting retention in OpenSIMPLE could be its entirely online delivery. Screening, enrolment and follow-up were done online without any face-to-face or telephone contact. It is possible that the initial intent to give participants the sense of self-management and privacy could actually be resulting in less commitment to the programme. This has previously been seen by other large-scale clinical trials using a fully remote online approach for depression (Anguera et al., 2016; Arean et al., 2016). Interestingly, in one of these studies, which delivered assessments and treatments exclusively through mobile devices, Anguera et al. (Anguera et al., 2016) found lower adherence among younger participants, which is in line with the findings of our study. This seems contradictory, as smartphone usage and ownership are higher among younger age groups (Andone et al., 2016; Montag et al., 2015; Poushter, 2016). However, engagement with e-mental health interventions in younger participants has already been described as a challenging issue in e-mental health interventions. For instance, Nicholas et al. found that young age was a significant predictor of attrition in a large 6-month RCT evaluating a web-based psychoeducational programme for BD (Nicholas et al., 2010; Proudfoot et al., 2012). Another similarity between this last study and OpenSIMPLE is the reasons given by participants for nonadherence. Among them, the fact that the programme reminded participants about their illness as well as the burden is especially important to consider when delivering more intensive programmes in shorter periods of time.

In contrast to our results, other studies evaluating e-mental health apps have identified several factors predictive of engagement other than age, including gender, socioeconomic factors, education and illness or symptoms severity (Anguera et al., 2016; Taki et al., 2017; Zeng et al., 2015).

In our study, none of the models explored showed a significant association with either manic or depressive symptoms. It is possible that symptomatic or cognitively impaired patients do not have the functionality levels required to enrol or reliably use Internet-based programmes. Further research is needed to investigate this.

In keeping with the above, it should be considered if smartphone apps can be used in mental health as adjunctive stand-alone self-management treatments or as an additional intervention within a multicomponent programme with face-to-face assessments and treatments. The majority of participants in our study were already receiving some kind of psychological treatment, which might have been a factor influencing retention. Regardless of this, any app design should be grounded on an evidence-based framework which has to provide a behavioural plan encouraging the users to engage with the app (Bakker et al., 2016). Moreover, the balance between duration, frequency and engagement requirements to deliver the programme's contents is one of the most important factors that might be considered to ensure retention.

One strategy that has been suggested to encourage app engagement is gamification. This method consists in adding elements of the most common video games rewarding and enjoyable mechanisms in non-video game contexts such as psychological programs (Brigham, 2015; Miller et al., 2014). In parallel, there is also an emergent interest in developing serious games as a potential strategy to engage users with e-mental health programmes (Lau et al., 2016; Stapleton, 2004). These are games which the main purpose is not entertainment *per se* but can be education, training or health improvement among other aims (Lau et al., 2016; Stapleton, 2004). Following this early evidence and users' suggestions, we implemented a basic gamification module in SIMPLE 1.5. However, the study findings suggest this was not perceived as helpful or engaging. Perhaps a more intensive and

immersive game experience could have an impact on retention; however, we need to be careful not to underestimate the seriousness of their clinical situation and the psychoeducational messages.

In addition to the gamification module, several other features were added to SIMPLE 1.5 based on the user-centred design (UCD) approach adopted early in the project (Hidalgo-Mazzei et al., 2015; Roth et al., 2014). Nonetheless, our results show that these features were only activated by a small percentage of users and the perceived helpfulness was generally low. Although in our smaller feasibility study this approach seemed to help attain an acceptable retention rate, the additional features didn't seem to engage a wider nor more diverse target population in this study (Hidalgo-Mazzei et al., 2016). A potential influencing factor may have been the direct extrapolation of users' feedback from one mental health centre in Spain only, perhaps wrongfully assuming worldwide applicability. While there are several successful examples of adopting this approach (Chiauzzi et al., 2015; Vilardaga et al., 2018), there are other studies reporting similar acceptability and retention rates using a top-down platform development (Biagianti et al., 2017). Nonetheless, we believe that this iterative process, if comprehensive and pragmatic enough, could provide essential information about users' preferences as well as the optimal balance between convenience and burden, which could ultimately increase satisfaction rates and potential favourable clinical outcomes.

Finally, we acknowledge that the role of a feasibility implementation study in parallel to an efficacy trial in the context of smartphone app validation might be a matter of debate. As the ultimate aim is to make e-mental health IBPs available to patients, we believe these kinds of implementation feasibility studies are an important step of the process. Bipolar illness may be one of the best disorder candidates for this type of approaches (Grande et al., 2016; Vieta et al., 2018), given, on the one hand, the severity and highly recurrent profile of the disease, and on the other hand the ability of many of these patients to benefit from psychoeducative interventions.

## Limitations

There are several methodological and practical limitations of this work that must be noted and generalizing results should be done with caution.

First, the screening, baseline and follow-up measures were administered using exclusively self-reported online methods which impeded reaching out back participants who dropped out to collect reasons for attrition or further comments about their experience with the programme. Furthermore, the accuracy and reliability of the information provided could not be verified, and this may have influenced the sample included and the secondary outcome results. For instance, the MDQ employed as a screening method has good sensitivity but low specificity, which could have resulted in the inclusion of participants who do not have a professional diagnosis of BD, but instead of other conditions such as borderline personality disorder (Zimmerman et al., 2011). However, this an issue also present in face-to-face interviews on routine clinical care (Ruggero et al., 2010; Zimmerman, 2016). Furthermore, clinical information such as illness years, previous episodes, comorbidities, hospital admissions and treatments received also relied only on self-report. Nevertheless, these data were similar to other clinical studies using face-to-face validated assessments and international treatment patterns. For example, there were high rates of antidepressants prescription in our sample of participants which was somewhat similar to other larger international studies (Samalin et al., 2016). This still seems contradictory taking into account the most recent treatment guidelines and consensus recommendations for BD (Goodwin et al., 2016; Pacchiarotti et al., 2013). The only exception on the similarity with other studies including patients with BD was the number of previous mood episodes, which was higher than expected; this could be a consequence of participants identifying reactive emotional fluctuations or subsyndromal symptoms with relapses. It also worth mentioning that our study had a low number of exclusion criteria in order to replicate an open

platform in a real world-setting of diverse participants. We tried to partially minimize this by assessing and reviewing, both with conditional algorithms and manual review, the consistency of every participant's screening and baseline responses.

Secondly, there was no alternative intervention or control group which could discriminate against a potential placebo effect in our study as it was not designed or aimed to demonstrate efficacy. Thirdly, we performed analyses to compare pre-post primary and secondary outcomes in the whole sample as well as between completers and non-completers. Although primary outcomes regarding satisfaction and usability were positive, it should be noted that this was predominantly among completers who might be more likely to report positive outcomes. Furthermore, even though some positive secondary clinical outcomes were found, these results should be taken with caution as most of them were based only in pre-post measures.

Finally, the attrition rate could limit the generalizability of the results as only about a third of the sample used the app for the entire duration of the programme and only about a half replied to the follow-up questionnaire. This resulted in skewed data, which we attempted to mitigate by implementing appropriate statistical methods. Further studies with larger samples could address this issue. Moreover, as it has already been demonstrated, passive behaviour information (i.e. without users input) captured from the smartphone usage and sensors could enhance the precision of clinical algorithms and could represent a paradigm shift in mood tracking methods (Faurholt-Jepsen et al., 2018, 2015; Hidalgo-Mazzei et al., 2018). The next version of SIMPLE (i.e. SIMPLE+) incorporates this technology based on smartphone usage patterns and sleep tracking capabilities to enable a better personalization of psychoeducational messages and avoid the burden of answering daily tests, thus addressing one of the main reasons for drop-out given by participants.



Regarding the limitations of the app itself, it was only available in Spanish which restricted the access to potential participants with different languages.

## Conclusion

The attrition rates of our implementation feasibility study delivering a large-scale psychoeducational programme for BD through smartphones were significant. We found positive outcomes regarding satisfaction and usability predominantly among completers, as well as perceived helpfulness and reported benefits to well-being and general health of all participants. The only variable significantly associated with retention was older age. In addition to proving efficacy, future studies should explore the optimal strategy to balance frequency, intensity and duration of these kinds of e-mental health programmes as well as to better understand user retention and engagement factors.

Upon overcoming the retentions issues and demonstrating efficacy, these platforms could become extremely cost-efficient tools for delivering psychoeducational contents to patients with BD globally due to the remarkably low set-up and maintenance costs.

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## Authors' contributions

DH, MR, CB, AM, EV and FC designed the protocol. DH and FC developed and maintained the project's website. SS and AG collaborated in the recruitment process. AG was in charge of giving online support to the users. AM, CB and MR gave advice during the data management and conducted the statistical analyses. DH, VN and LS prepared the first draft of the manuscript which was subsequently reviewed and improved by SS, VP, AY, EV and FC.

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use of laboratory animals. The protocol of the project was approved in accordance to the local spanish laws (Ley orgánica de Protección de Datos de Carácter Personal (15/1999). Additionally, the study protocol was evaluated and approved Hospital Clínic of Barcelona (HCB/2016/0403) and the Hospital del Mar - IMIM: Institut Hospital del Mar d'Investigacions Mèdiques (2016/6764/I). This report represents independent research partially funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health.

## Conflict of Interest

DH, AM, MR, EV and FC have designed the SIMPLE smartphone application mentioned in this study. The authors declare no other conflict of interests regarding this manuscript. The authors do not have any economic interests in the SIMPLE application, its use or copyrights.

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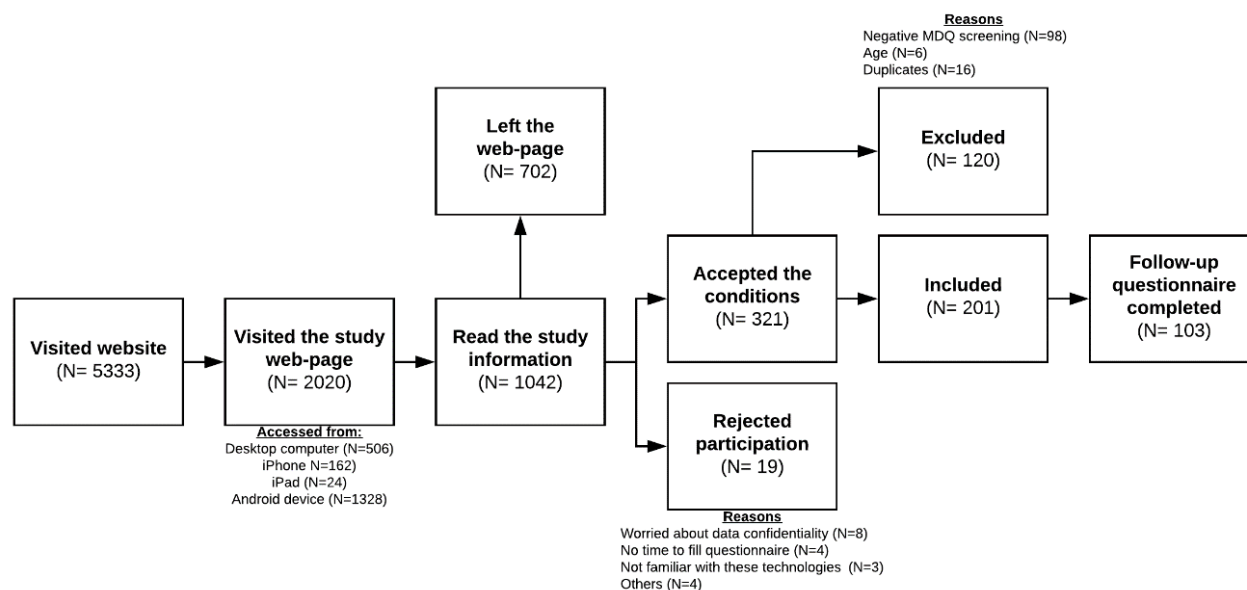
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Figure 1. Study process flowchart



MDQ= Mood disorders questionnaire.

Figure 1. The flowchart describes the number of subjects who visited the project's website and the number of users who actually viewed the study web-page alongside the devices from which they accessed it. Subsequently the flowchart describes those users who went on to read the information about the study and conditions to participate. Reasons reported by users who didn't want to participate in the study are also listed. Finally, potential participants who were excluded and their reasons are described, as well as the number of participants included in the study and those who responded the 6-month follow-up questionnaire.

\*Figure 2. OpenSIMPLe study 6-months users retention

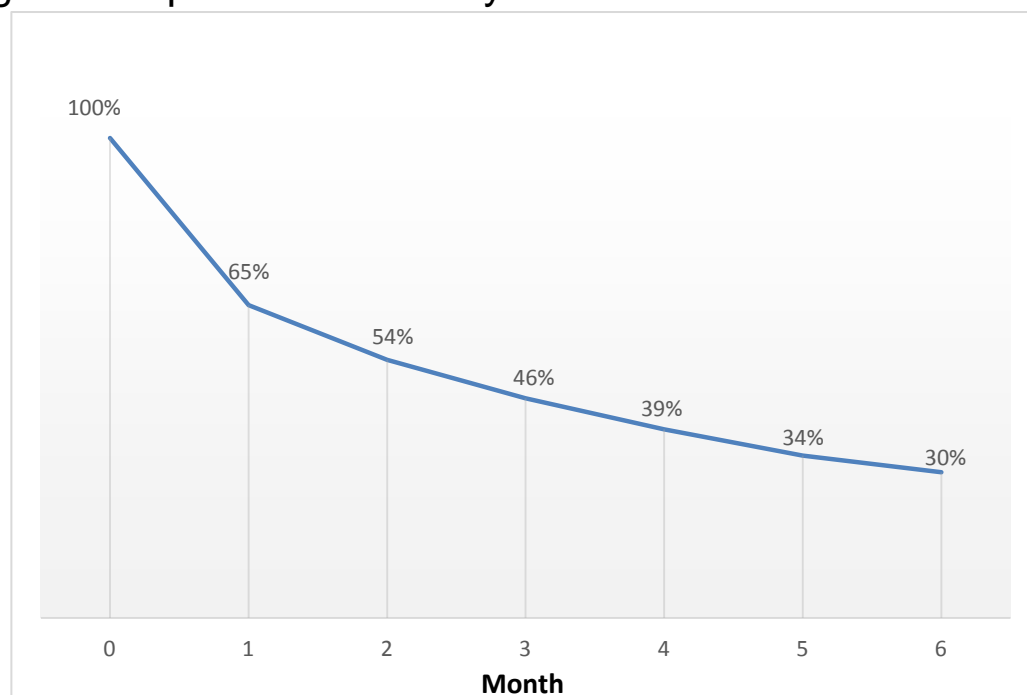


Figure 2. The figure shows the percentage of active users retention in each of 6 months of the study.

Figure 3. OpenSIMPLe programme components perceived helpfulness

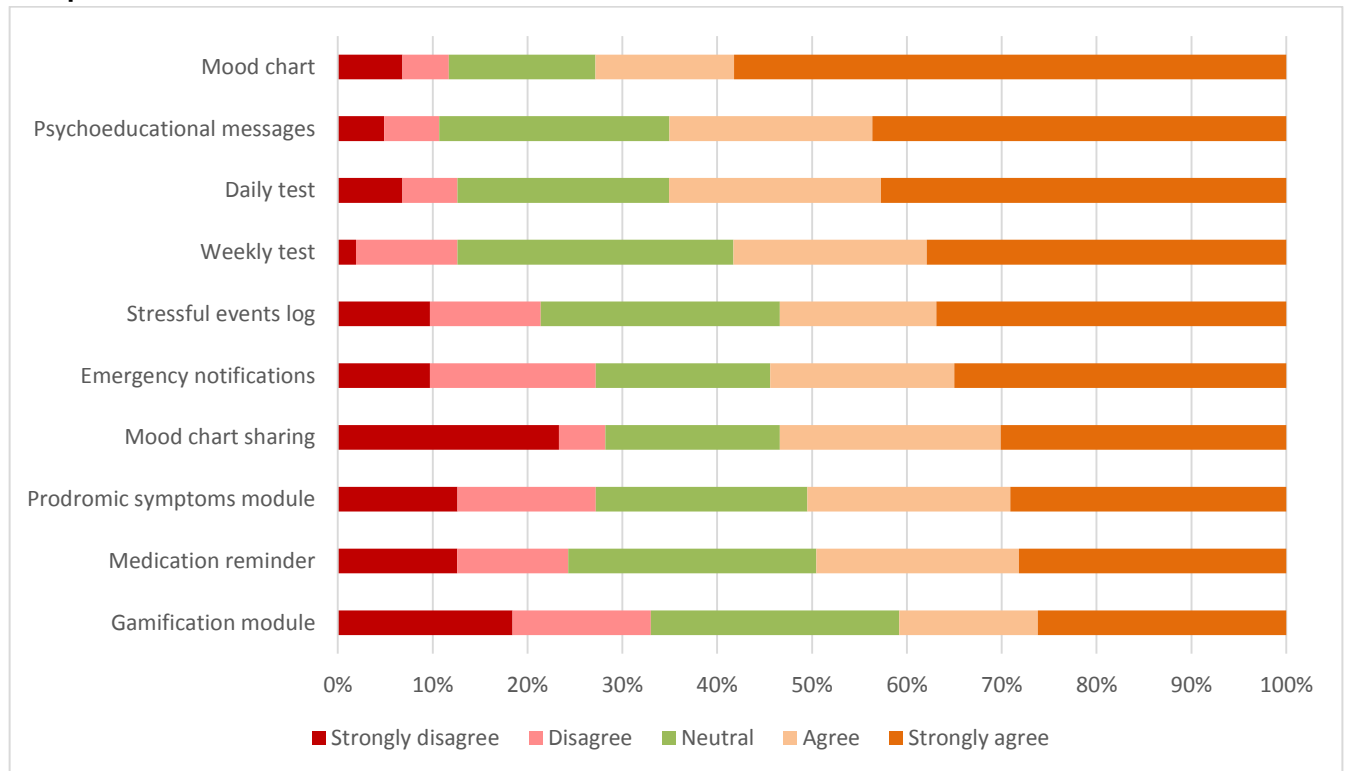


Figure 3. The bars denote the percentage of perceived helpfulness of each component of the programme by the users who responded to the follow-up questionnaire. Right areas of the bars shows stronger agreement that the component was helpful while left areas stronger disagreement.



<b>Table 1. Baseline sociodemographic characteristics (N=201)</b>		
	<b>Mean</b>	<b>SD</b>
<b>Age</b>	36.59	11.0
	<b>N</b>	<b>Percentage</b>
<b>Gender</b>		
Male	74	36.8
Female	127	63.2
<b>Ethnicity</b>		
Latin-american	121	60.5
Caucasian	77	38.5
African	1	0.5
Asian	1	0.5
<b>Educational level</b>		
Low	8	4.0
Medium	67	33.3
High	126	62.7
<b>Marital status</b>		
Single	93	46.2
Married/Cohabiting	67	33.3
Divorced/Separated	32	15.9
<b>Employment status</b>		
Student	32	15.9
Employed	84	41.8
Unemployed	38	18.9
Permanent disability leave	22	10.9
Temporary disability leave	20	10
Retired	5	2.5
<b>Housing status</b>		
Home owner/renter	106	52.8
Shared home	90	44.8
Institution/residence	5	2.4

SD = Standard deviation

Table 1. The table details the baseline sociodemographic characteristics of the participants.

<b>Table 2. Baseline clinical characteristics and treatments (N=201)</b>		
	<b>N</b>	<b>Percentage</b>
<b>Comorbidity</b>		
Medical comorbidities	123	61.2
Anxiety disorders	75	37.3
Personality disorders	41	20.4
Substance use disorders (SUD)	26	12.9
Post-traumatic stress disorder (PTSD)	11	5.5
Any psychiatric comorbidity	123	61.2
<b>Family History of psychiatric disorder</b>		
None	50	24.9
First degree	73	36.3
Second degree	44	21.9
Third degree	34	16.9
<b>Current pharmacological and non-pharmacological treatments</b>		
Mood stabilizers	156	77.6
Antipsychotics	129	64.1
Antidepressants	98	48.7
Benzodiazepines	97	48.2
Electroconvulsive therapy (ECT)	1	0.5
Psychological treatment	143	71.1
<b>Previous non-pharmacological treatments</b>		
Psychological treatment	178	88.5
Electroconvulsive therapy (ECT)	10	5
	<b>Mean</b>	<b>SD</b>
<b>Illness course</b>		
Manic/Hypomanic episodes	6.9	3.3
Depressive episodes	6.2	3.6
Total episodes	13.1	5.9
Age of onset (years)	27.9	9.6
Illness years	7.9	8.1
Episode density	0.8	1.2
Previous hospital admissions due to an episode	1.3	1.9
Previous suicide attempts	1.2	1.7

SD = Standard deviation

Table 2: The table details the baseline clinical characteristics and treatments of the participants.